

Remarks

The Rejection of Claims 1-17 Under 35 U.S.C. § 112, first paragraph

Claims 1-17 remain rejected under 35 U.S.C. § 112, first paragraph, as insufficiently described. Applicants respectfully traverse the rejection.

The first paragraph of 35 U.S.C. § 112 requires that the specification provide a written description of a claimed invention sufficient to convey to those skilled in the art that the applicants possessed the claimed subject matter as of the filing date sought. *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 U.S.P.Q.2d 1111, 1117 (Fed. Cir. 1991). The specification must describe in detail, however, only that which is “new or not conventional in the art.” M.P.E.P. § 2163(II)(A)(3)(a), citing *Hybritech v. Monoclonal Antibodies*, 802 F.2d 1367, 1384, 231 U.S.P.Q. 81, 94 (Fed. Cir. 1986). Whether the specification meets the written description requirement for the claimed invention is a question of fact. *Vas-Cath*, 935 F.2d at 1563, 19 U.S.P.Q.2d at 1116.

The first step in a proper written description analysis is a determination of the scope of the subject matter of each claim. *Vas-Cath Inc.*, 935 F.2d at 1563-64; 19 U.S.P.Q.2d at 1116. Independent claim 1 is directed to a pair of cells. The cells are isogenic but for a gene of interest and a gene encoding a fluorescent protein. One cell of the pair comprises a gene which encodes a first fluorescent protein having a first absorption spectrum and a first emission spectrum. The other cell of the pair comprises a gene which encodes a second fluorescent protein having a second absorption spectrum and a second emission spectrum. Either the absorption spectra and/or the emission spectra of the two fluorescent proteins are different.

The Final Office Action acknowledges that the specification need not explicitly describe genes encoding fluorescent proteins because such genes are conventional in the art. Final Office

Action at page 4, last paragraph. But the Final Office Action asserts that the specification does not adequately describe either the recited gene of interest or the recited pair of cells. This assertion is based on an improper claim construction and is not supported by controlling legal precedent.

The Final Office Action misconstrues claim 1 as actually claiming the gene of interest: “Further, applicant’s claim that they are not claiming new genes or [sic; of] interest is incorrect, because in order to make the isogenic cell lines one of the cells must contain a mutated ‘gene of interest.’ Said mutated ‘gene of interest’ is the core of the invention as this is the altered gene that makes the pair of cells an isogenic pair of cells.” Final Office Action at page 5, lines 2-5. This claim construction and characterization of the invention is incorrect. Applicants do not claim the gene of interest; Applicants claim the recited pair of cells.

The specification adequately describes the genus of claimed cell pairs if the description permits one of skill in the art to visualize or recognize members of the genus. *University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 1559, 43 U.S.P.Q.2d 1398, 1406 (Fed. Cir. 1997). See also *Enzo Biochem, Inc. v. Gen-Probe Incorporated*, 296 F.3d 1316, 1327, 63 U.S.P.Q.2d 1609, 1615 (Fed. Cir. July 15, 2002) (“the language of the specification, to the extent possible, must describe the claimed invention so that one skilled in the art can recognize what is claimed”). The specification contains the following specific teachings with respect to cells and genes of interest:

- [30] Any type of mammalian cell that can be maintained in a culture can be transfected and used to generate a cell with specific genetic alterations. These cells include, but are not limited to, primary cells, such as fibroblasts, myoblasts, leukocytes, hepatocytes, endothelial cells, and dendritic cells, as well as cell lines (e.g., NCI-BL2126, Hs 578Bst, HCC1954 BL, Hs 574.Sk, Hs888Lu, which are available from the American Type Culture Collection, 10801 University Boulevard,

Manassas, VA 20110-2209). Established tumor cell lines, such as HT29, SW480, HCT116, DLD1, MCF-7, HL-60, HeLa cell S3, K562, MOLT-4, Burkitt's lymphoma Raji, A549, G361, M12, M24, M101, SK-MEL, U-87 MG, U-118 MG, CCF-STTG1, or SW1088 can be used. Preferred cells include human cells, preferably human tumor cells, more preferably human colon tumor cells and human breast tumor cells.

* * *

- [32] Any means known in the art to create cells with defined alterations in specific genes may be used. For example, homologous recombination can be used to generate an isogenic clone that differs from its parent cell only in a single mutant gene (Capechi, *Science*, 244:1288-92, 1989).

As these teachings in the specification indicate, neither the recited “gene of interest” nor the cell types of the claimed cell pair are new elements in the art. Moreover, as indicated by its use in numerous patents, the term “gene of interest” is a term understood in the art. See page 3 of the response filed May 20, 2004. Applicants’ use of the term “gene of interest” merely reflects the fact that the claimed pair of isogenic cells can differ with respect to any gene in which one practicing the invention is interested. By the September 1, 2001 filing date of this application, those of skill in the art knew of thousands of genes. None of these thousands of genes was “new” when the application was filed; thus the specification need not describe these genes to permit one skilled in the art to visualize or recognize a “gene of interest” or a the claimed pair of cells. *Hybritech*, 802 at 1384, 231 U.S.P.Q. at 94.

Applicants acknowledge that “gene of interest” encompasses genes not known at the time of filing. That the claimed pair of cells may differ as to a gene not yet discovered is not a basis for a written description rejection. The patent law does not require that the specification describe later-discovered species which would fall within a recited genus. *Rexnord Corporation v. Laitram Corporation*, 274 F.3d 1336, 1344, 60 U.S.P.Q.2d 1851, 1856 (Fed. Cir. 2001) (“Our case law is clear that an applicant is not required to describe in the specification every

conceivable and possible future embodiment of his invention.”). The fact that the “gene of interest” encompasses possible later-discovered genes does not support the assertion that the specification’s description of the invention is not adequate.

The facts of record demonstrate that, if the claims are properly construed and if the specification is considered from the point of view of one skilled in the art, the specification plainly satisfies the legal standard for a written description of the claimed invention. Neither of the Office Actions in this case cites any evidence to support the assertion that one skilled in the art would not have been able to visualize the genus of “genes of interest” or the genus of the claimed cell pairs. If the rejection is maintained, Applicants request that the Examiner withdraw the finality of this action and specifically point out the evidence relied upon so that Applicants have the opportunity to address this evidence. If the Examiner is relying on personal information as a basis for the rejection, Applicants request that the Examiner provide an affidavit under 37 C.F.R. § 1.104(d)(2).

Applicants respectfully request withdrawal of the rejection.

The Rejection of Claims 1-17 Under 35 U.S.C. § 103(a)

The Final Office Action maintains the rejection of claims 1-17 under 35 U.S.C. § 103(a) over Waldman, US 2002/0132340 (“Waldman”) in view of Kain, *Drug Discovery Today* 4, 304-12, 1999 (“Kain”). Applicants respectfully traverse the rejection.

The U.S. Patent and Trademark Office bears the initial burden of establishing a *prima facie* case of obviousness. The *prima facie* case requires three showings:

First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

M.P.E.P., 8th ed., § 2142. The Final Office Action still has not made a *prima facie* case of obviousness for claims 1-17 because the asserted motivation to have combined the teachings of the cited references is legally insufficient.

The Office Action cites Waldman as teaching “a pair of isogenic cell lines comprising beta-catenin, wherein said cells are heterozygous for a wild-type and a mutant beta catenin gene, or hemizygous for wild-type beta-catenin, hemizygous for mutant beta-catenin, homozygous for wild-type beta catenin and homozygous for mutant beta-catenin.” Final Office Action at page 6, first full paragraph. The Final Office Action cites Kain as teaching the use of combinations of fluorescent proteins to quantify mixed cell populations. Final Office Action at page 7, first full paragraph. The asserted motivation for combining these teachings is that Waldman “suggests the use of a fluorescent signal as a detectable phenotype.” Final Office Action at page 7, second paragraph.

Applicants explained in the previous response why the asserted motivation is insufficient for one of ordinary skill in the art to have combined the cited references when the teachings of those references are properly considered as a whole and compared with the subject matter of the rejected claims. *Graham v. John Deere* 383 U.S. 1, 17 (1966). See the discussion on pages 5-9 of the response filed May 20, 2004. The Final Office Action improperly characterizes Applicants' argument as follows:

Applicant argues that the asserted motivation is insufficient for one of ordinary skill n [sic; in] the art to have combined the cited references and that the teachings of the cited references must be combined as a whole and compared with the subject matter of the rejected claims (THIS HAS TO DO WITH TEACHING AGAINST). This has been considered but not found persuasive. When combined as a whole there is nothing in the individual references which would "teach against" the combination. Applicant argues that the general teachings of the references be looked at to the extent that the specific technical teachings be ignored.

Id. Applicants did not argue that specific teachings in the cited references should be ignored; rather, Applicants' May 20 response urged that these teachings be considered in the context of the complete teachings of each reference. This analysis is not optional. It is a required inquiry in assessing whether a claimed invention is obvious. *Graham*, 383 at 17 ("Under § 103, the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved."). See also *In re Kotzab*, 217 F.3d 1365, 1371, 55 U.S.P.Q.2d (BNA) 1313, 1317 (Fed. Cir. 2000) ("[s]tatements [in a prior art reference] cannot be viewed in the abstract. Rather, they must be considered in the context of the teaching of the entire reference."). Instead of properly carrying out this analysis, the U.S. Patent and Trademark Office has ignored the complete teachings of the cited references in favor of improperly picking and choosing isolated elements of the references.

The U.S. Patent and Trademark Office still has not established a legally sufficient motivation for the ordinary artisan to have combined the cited teachings of Waldman and Kain. Thus, no *prima facie* case of obviousness has been established.

Applicants respectfully urge the Office to use the proper legal standard, reconsider the arguments in Applicants' May 20 response, and withdraw the rejection.

The Rejection of Claims 1-3 and 11-20 Under 35 U.S.C. § 103(a)

Claims 1-3 and 11-20 stand rejected under 35 U.S.C. § 103(a) as obvious over Shirasawa *et al.*, *Science* 260, 85-88, 1993 ("Shirasawa") in view of Vande Woude *et al.*, U.S. Patent 5,645,988 ("Vande Woude") and Kain. Applicants respectfully traverse the rejection.

The Final Office Action cites Shirasawa as teaching isogenic cell lines that differ in alleles of K-Ras; it cites Vande Woude as teaching cancer cells that "differ as to the presence of a particular DNA sequence," including K-ras-2. Final Office Action at page 10, first full paragraph. The Final Office Action cites Kain as discussed above. Paragraph bridging pages 10 and 11 of the Final Office Action. The Final Office Action asserts it would have been obvious to combine these teachings "in order to use the color of the fluorescent protein as a detectable phenotype of the cell in order to measure the effects of toxic agent on cell [sic] which comprise the oncogenic Ras mutations as taught by Wander woude [sic] et al." Page 11, first full paragraph.

As with the rejection of claims 1-17 discussed above, Applicants' previous response explained that the asserted motivation is insufficient for one of ordinary skill in the art to have combined the cited references when the teachings of those references are properly considered as a whole and compared with the subject matter of the rejected claims. *Graham v. John Deere* 383

U.S. 1, 17 (1966). See the discussion on pages 10-12 of the response filed May 20, 2004. Here, too, the Final Office Action uses an improper standard and dismisses Applicants' argument:

Applicant somehow reasons that one of skill in the art should ignore specific technical information taught by each of the references and just look at each of the references as a whole. This has been considered but not found persuasive. One of skill in the art would be motivated to combine the teachings in order to make technical advances, legally sufficient motivation is irrelevant to those who are routineers.

Final Office Action at page 12, lines 9-13.

The U.S. Patent and Trademark Office's position articulated in the Final Office Action is plainly contrary to Supreme Court precedent. It is black letter law that the teachings of the cited references must be considered as a whole and that a *prima facie* case of obviousness requires demonstration of a legally sufficient motivation to have combined the cited teachings. Applicants respectfully urge the Office to use the proper legal standard, reconsider the arguments in Applicants' May 20 response, and withdraw the rejection.

Respectfully submitted,
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